

Applicants: Jingrong Cao et al.  
Application No.: 10/696,862

### REMARKS

#### The Claim Amendments

Claims 1, 48, and 50 have been amended such that the independent definitions of Ar<sup>1</sup> and Ar<sup>2</sup> have been separated and the alternative embodiment wherein Ar<sup>1</sup> is a nitrogen-containing heterocyclic ring has been deleted. In addition, the substituents containing an oxidized phosphorus atom have been deleted from the definitions of linker moieties. Support for these amendments is found in the original claims and the corresponding specification text.

Claims 9, 10, 36, and 45 have been amended to correspond these claims to amended claim 1. Specifically, these claims do not recite compounds in which Ar<sup>1</sup> is a nitrogen-containing ring.

Claims 24, 36, 37, and 42 have been amended to correct informalities. Specifically, a dashed line has been inserted before bonded radicals to maintain consistency within each of these claims.

Claims 34 and 35 have been amended to change their dependencies from claim 1 to claim 9 and claims 38, 39, and 40 have been amended to change their dependencies from claim 1 to claim 16. These amendments are necessitated by ring definitions used in dependent claims 36 for Ar<sup>1</sup> and in dependent claims 41 and 42 for Ar<sup>2</sup>. Support for these amendments is found in the original claims and the corresponding specification text.

Claims 47 and 51 have been amended to recite a composition or a method, respectively, that includes an additional therapeutic agent selected from specific chemotherapeutic or anti-proliferative agents, anti-inflammatory agents, or agents for treating cardiovascular disease. The amended claims thus corresponds the additional agents to the diseases or disorders recited by amended claim 50. These amendments find support in paragraphs [00149] and [00150] on pages 104-105 of the specification.

Claim 48 has been amended to recite a method of inhibiting kinase activity *in*

Applicants: Jingrong Cao et al.  
Application No.: 10/696,862

*vitro* in a biological sample selected from a cell culture or extract thereof, biopsied material obtained from a mammal or an extract thereof, saliva, urine, feces, semen, or tears with a compound of the invention. Support for this amendment is found in paragraph [00154] on page 106 of the specification.

Claims 50 and 53 have been amended to recite specific diseases or disorders treated by the compounds of the invention. Support for these amendments is found in paragraphs [00142] to [00144] on pages 102-103 of the specification.

None of these amendments adds new matter. Their entry is requested.

#### The Response

##### *Rejection under 35 U.S.C. § 112, second paragraph*

The Examiner has rejected claims 1-56 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Specifically, the Examiner states that the recitation of linker moieties as -PO- and -POR- makes the valency of these linkers unclear. Applicants have deleted oxidized phosphorus moieties from the definitions of linkers in claims 1, 48, and 50. Accordingly, applicants request that the Examiner withdraw this objection.

##### *Rejection under 35 U.S.C. § 112, first paragraph*

The Examiner has rejected claims 47-53 under 35 U.S.C. § 112, second paragraph. The Examiner alleges that applicants have not provided sufficient evidence that establishes that the disclosure was enabling for one skilled in the art at the time of filing for the entire scope of the methods of use recited in the instant claims. In addition, the Examiner asserts that claims 47-53 are reach-through claims that are drawn to mechanistic functionality and thereby reach through to any or all diseases, disorders, or conditions for which they lack written description and enabling disclosure. Applicants traverse.

Claim 47 recites a composition of the invention and is therefore should not be

Applicants: Jingrong Cao et al.  
Application No.: 10/696,862

rejected under 35 U.S.C. § 112 as a method of treatment claim. Applicants respectfully request that the Examiner's rejection of claim 47 be withdrawn.

Amended claims 48 and 49 recite a non-therapeutic method of inhibiting kinase activity in a biological sample selected from a cell culture or extract thereof, biopsied material obtained from a mammal or an extract thereof, saliva, urine, feces, semen, or tears. These amended claims do not recite an *in vivo* method of treating human or animal diseases or disorders and are instead directed to specific *in vitro* tests. Thus, applicants respectfully request that the Examiner withdraw his rejection of claims 48 and 49.

Amended claim 50 and claims 51-56 dependent thereon recite specific diseases or disorders that are treated by compositions of the invention, including various proliferative and cardiovascular diseases, as well as Alzheimer's disease, allergies, asthma, and diabetes. In the previous response, applicants made of record references available at the time of filing that provide a reasonable correlation between the inhibitors of the invention, the data showing their inhibitory activity, and the use of these compounds to treat each of the various diseases or disorders recited by the amended claims. Therefore, applicants respectfully request that the Examiner withdraw his objection to these claims under 35 U.S.C. § 112.

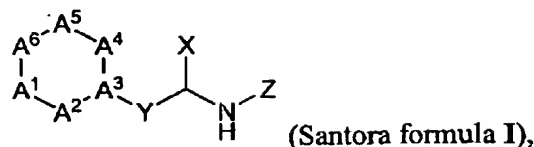
*Rejection under 35 U.S.C. § 103(a)*

The Examiner has again rejected claims 1-47 and 50-53 under 35 U.S.C. § 103(a) as allegedly being obvious over Santora et al., PCT Publication No. WO 02/14311 (hereafter, "Santora")

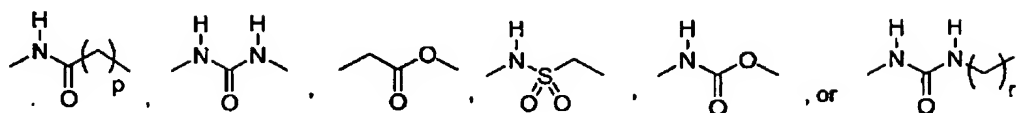
The Examiner asserts that the compounds taught in Examples 1-233 of Santora are equivalent to those compounds that are generically recited having the formula:

Applicants: Jingrōng Cao et al.

Application No.: 10/696,862

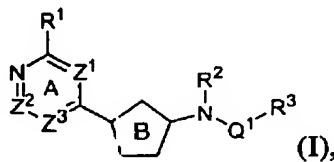


where Y is:



The Examiner then alleges that it would have been obvious to one having ordinary skill in the art to make the compounds of the instant invention and expect those compounds to possess the uses taught by the art in view of the “equivalency” of Examples 1-233 to the generic formulae of Santora. In particular, the Examiner asserts that there is generic overlap between the compounds of the instant application and those of Santora, where Y is -NHC(O)-(CH<sub>2</sub>)<sub>p</sub>. Applicants traverse.

There is no overlap between the compounds amended claims and those of Santora, since Santora recites compound of Santora formula I wherein X and Y taken together form a nitrogen-containing ring selected from an optionally substituted 5-6 membered heterocyclyl or an optionally 5-6 membered heterocyclyl fused with a phenyl group. In contrast, the amended claims of the instant application recite compounds having the formula:



wherein Q<sup>1</sup> is -CO-, -SO<sub>2</sub>-, or -SO<sub>2</sub>NR- and R<sup>3</sup> is Q<sup>2</sup>-Ar<sup>1</sup>, where Q<sup>2</sup> is a bond or a C<sub>1-6</sub> alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by -S-, -O-, -CS-, -CO<sub>2</sub>-, -OCO-, -CO-, -COCO-, -CONR'-, -NR'CO-, -NR'CO<sub>2</sub>-, -SO<sub>2</sub>NR'-, -NR'SO<sub>2</sub>-, -CONR'NR'-, -NR'CONR'-,

Applicants: Jingrong Cao et al.  
Application No.: 10/696,862

-OCONR<sup>1</sup>-, -NR<sup>1</sup>NR<sup>2</sup>-, -NR<sup>1</sup>SO<sub>2</sub>NR<sup>2</sup>-, -SO-, or -SO<sub>2</sub>-, and Ar<sup>1</sup> is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from oxygen or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from oxygen or sulfur.

Therefore, the amended claims of the instant application do not recite compounds in which Ar<sup>1</sup> is a nitrogen-containing heterocycle. Accordingly, the Examiner's obviousness rejection has been obviated and applicants respectfully request that the Examiner withdraw his rejection under 35 U.S.C. § 103(a).

#### Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying arguments, and allow the claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the Examiner contact the undersigned at his convenience.

Respectfully submitted,



Daniel A. Pearson (Reg. No. 58,053)  
Agent for Applicants  
c/o Vertex Pharmaceuticals Incorporated  
130 Waverly Street  
Cambridge, MA 02139-4242  
Tel.: (617) 444-6790  
Fax.: (617) 444-6483